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PCT

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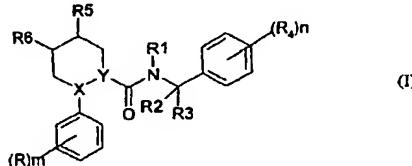
(30) Priority Data:  
0203021.1 8 February 2002 (08.02.2002) GB  
0203019.5 8 February 2002 (08.02.2002) GB(71) Applicant (for all designated States except US): GLAXO  
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(75) Inventors/Applicants (for US only): ALVARO, Giuseppe  
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2, I-37135 Verona (IT). PAIO, Alfredo [IT/IT]; GlaxoSmithKline SpA, Via Alessandro Fleming 2, I-37135 Verona (IT). PONTIROLI, Alessandro [IT/IT]; GlaxoSmithKline SpA, Via Alessandro Fleming 2, I-37135 Verona (IT). SPADA, Simone [IT/IT]; GlaxoSmithKline SpA, Via Alessandro Fleming 2, I-37135 Verona (IT). TRANQUILLINI, Maria, Elvira [IT/IT]; GlaxoSmithKline SpA, Via Alessandro Fleming 2, I-37135 Verona (IT).

(74) Agent: THOMPSON, Clive, Beresford; CN925.1, 980  
Great West Road, Brentford, Middlesex TW7 9GS (GB).(81) Designated States (national): AB, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,  
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,  
MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE,  
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[Continued on next page]

(54) Title: PIPERIDYLCARBOXAMIDE DERIVATIVES AND THEIR USE IN THE TREATMENT OF TACHYKININ-MEDIATED DISEASES



WO 03/066589 A1

(57) Abstract: The present invention relates to piperidine derivatives of formula (I) wherein R represents halogen or C<sub>1-4</sub>alkyl; R<sub>1</sub> represents hydrogen or C<sub>1-4</sub>alkyl; R<sub>2</sub> represents hydrogen, C<sub>1-4</sub>alkyl or R<sub>3</sub> together with R<sub>3</sub> represents C<sub>3-7</sub>cycloalkyl; R<sub>3</sub> represents hydrogen, C<sub>1-4</sub>alkyl, C<sub>3-7</sub>cycloalkyl or C<sub>3-6</sub>alkenyl; or R<sub>1</sub> and R<sub>3</sub> together with nitrogen and carbon atom to which they are attached respectively represent a 5 to 6 membered heterocyclic group; R<sub>4</sub> represents trifluoromethyl, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, trifluoromethoxy or halogen; R is hydrogen and R is NR<sub>7</sub>R<sub>8</sub> or R<sub>3</sub> is NR<sub>8</sub>R<sub>9</sub> and R<sub>8</sub> is hydrogen; R<sub>7</sub> represents hydrogen or C<sub>1-4</sub>alkyl or R<sub>7</sub> and R<sub>8</sub> together with nitrogen to which they are attached are a saturated 5 to 7 membered heterocyclic group containing oxygen; R<sub>8</sub> represents hydrogen, phenyl, C<sub>3-7</sub>cycloalkyl, (CH<sub>2</sub>)<sub>p</sub>C(O)NR<sub>10</sub>R<sub>11</sub>, a saturated 5 to 7 membered heterocyclic group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen and optionally substituted by C<sub>1-4</sub>alkyl, S(O)<sub>2</sub>C<sub>1-4</sub>alkyl or C(O)C<sub>1-4</sub>alkyl, a 5 membered heteroaryl group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen and optionally substituted by C<sub>1-4</sub>alkyl S(O)<sub>2</sub>C<sub>1-4</sub>alkyl or C(O)C<sub>1-4</sub>alkyl or R<sub>8</sub> represents a 6 membered heteroaryl group containing 1 to 3 nitrogen atoms and optionally substituted by C<sub>1-4</sub>alkyl, S(O)<sub>2</sub>C<sub>1-4</sub>alkyl or C(O)C<sub>1-4</sub>alkyl; or R<sub>8</sub> is a C<sub>1-6</sub>alkyl group optionally substituted by one or two groups selected from fluorine, phenyl (optionally substituted by C<sub>1-4</sub>alkyl, C(O)C<sub>1-4</sub>alkyl or halogen), =O, C<sub>3-7</sub>cycloalkyl, hydroxy, amino, dimethylamino, aminocarbonyl, C<sub>1-4</sub>alkoxy or trifluoromethyl; R<sub>9</sub> is hydrogen, C<sub>1-4</sub>alkyl or R<sub>9</sub> and R<sub>10</sub> together with nitrogen to which they are attached are a 5 to 7 membered heterocyclic group optionally containing another heteroatom selected from oxygen, sulphur and nitrogen and optionally substituted by one or two groups selected from C<sub>1-4</sub>alkyl, =O, S(O)<sub>2</sub>C<sub>1-4</sub>alkyl, C(O)C<sub>1-4</sub>alkyl or C(O)C<sub>1-4</sub>alkyl; R<sub>10</sub> and R<sub>11</sub> are independently hydrogen or C<sub>1-4</sub>alkyl group; X represents a nitrogen atom and Y is CH or X represents CH and Y is nitrogen; m is zero or an integer from 1 to 3; n is an integer from 1 to 3; p is zero, 1 or 2; and pharmaceutically acceptable salts and solvates thereof; the process for their preparation and their use in the treatment of conditions mediated by tachykinins.

BEST AVAILABLE COPY

Received 19 MAG 2003

## PATENT COOPERATION TREATY

VERONA INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

GLAXO GROUP LIMITED  
 Attn. Thompson, C. B.  
 Glaxo Wellcome House  
 Berkeley Avenue  
 Greenford, Middlesex UB6 0NN  
 UNITED KINGDOM

GlaxoSmithKline  
 Corporate

Received BRENTFORD

16 MAY 2003

ATTY:

IPM

ATTY CH

NOTIFICATION OF TRANSMITTAL OF  
 THE INTERNATIONAL SEARCH REPORT  
 OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing  
(day/month/year)

16/05/2003

Applicant's or agent's file reference

PI4749

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/GB 03/00499

International filing date

05/02/2003

Applicant

GLAXO GROUP LIMITED

1.  The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

## Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO  
 34, chemin des Colombettes  
 1211 Geneva 20, Switzerland  
 Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2.  The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3.  With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Further action(s): The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for International preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority  
 European Patent Office, P.B. 5818 Patentlaan 2  
 NL-2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Laura Fernández Gómez

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the International preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before International publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the International application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

#### What documents must/may accompany the amendments?

Letter (Section 205(b));

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the International application is English, the letter must be in English; if the language of the International application is French, the letter must be in French.

## NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]: "Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]: "Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]: "Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or "Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]: "Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the International application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(s), first sentence).

### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>PI4749</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/GB 03/00499</b>	International filing date (day/month/year) <b>05/02/2003</b>	(Earliest) Priority Date (day/month/year) <b>08/02/2002</b>
Applicant <b>GLAXO GROUP LIMITED</b>		
<p>This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.</p> <p>This International Search Report consists of a total of <u>7</u> sheets.  <input checked="" type="checkbox"/> It is also accompanied by a copy of each prior art document cited in this report.</p>		
<p>1. <b>Basis of the report</b></p> <p>a. With regard to the <b>language</b>, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.</p> <p><input type="checkbox"/> the International search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).</p> <p>b. With regard to any <b>nucleotide and/or amino acid sequence</b> disclosed in the international application, the international search was carried out on the basis of the sequence listing :</p> <p><input type="checkbox"/> contained in the international application in written form.</p> <p><input type="checkbox"/> filed together with the international application in computer readable form.</p> <p><input type="checkbox"/> furnished subsequently to this Authority in written form.</p> <p><input type="checkbox"/> furnished subsequently to this Authority in computer readable form.</p> <p><input type="checkbox"/> the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.</p> <p><input type="checkbox"/> the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished</p> <p>2. <input checked="" type="checkbox"/> <b>Certain claims were found unsearchable</b> (See Box I).</p> <p>3. <input type="checkbox"/> <b>Unity of invention is lacking</b> (see Box II).</p> <p>4. With regard to the <b>title</b>,</p> <p><input type="checkbox"/> the text is approved as submitted by the applicant.</p> <p><input checked="" type="checkbox"/> the text has been established by this Authority to read as follows: <b>PIPERIDYL CARBOXAMIDE DERIVATIVES AND THEIR USE IN THE TREATMENT OF TACHYKININ-MEDIATED DISEASES</b></p> <p>5. With regard to the <b>abstract</b>,</p> <p><input checked="" type="checkbox"/> the text is approved as submitted by the applicant.</p> <p><input type="checkbox"/> the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.</p> <p>6. The figure of the <b>drawings</b> to be published with the abstract is Figure No.</p> <p><input type="checkbox"/> as suggested by the applicant.</p> <p><input type="checkbox"/> because the applicant failed to suggest a figure.</p> <p><input type="checkbox"/> because this figure better characterizes the invention.</p> <p style="text-align: right;"><input checked="" type="checkbox"/> None of the figures.</p>		

Form PCT/ISA/210 (first sheet) (July 1998)

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/00499

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D211/58 C07D401/04 C07D405/12 A61K31/451 A61K31/4525  
 A61K31/5377 A61K31/497 A61P25/22 A61P25/24

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, EPO-Internal

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 02 32867 A (GLAXO GROUP LTD ; TRANQUILLINI MARIA ELVIRA (IT); MARAGNI PAOLO (IT) 25 April 2002 (2002-04-25) cited in the application page 8, line 7 -page 12, line 26; claims ---	1-15
X	WO 97 16440 A (JANSSEN PHARMACEUTICA NV ; JANSSENS FRANS EDUARD (BE); SOMMEN FRANC 9 May 1997 (1997-05-09) cited in the application page 17, line 10 -page 19, line 8; claims 1,4,12,14 ---	1-15
X	WO 97 24324 A (JANSSEN PHARMACEUTICA NV ; JANSSENS FRANS EDUARD (BE); SOMMEN FRANC 10 July 1997 (1997-07-10) page 13, line 28 -page 15, line 26; claims 1,7,8 ---	1-15
	---	-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the International filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the International filing date but later than the priority date claimed

- \*T\* later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*G\* document member of the same patent family

Date of the actual completion of the international search

7 May 2003

Date of mailing of the International search report

16/05/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Hanisch, I

1

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/00499

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 532 456 A (CIBA GEIGY AG) 17 March 1993 (1993-03-17) page 4, line 55 -page 5, line 24; claims 1,118-120; examples 10,16 ---	1-15
A	WO 99 37304 A (BURNS CHRISTOPHER J ;CHOI SLEDESKI YONG MI (US); LAU WAN F (US); P) 29 July 1999 (1999-07-29) cited in the application page 230, line 10 - line 15; claims 1,27,28,48,65 ---	1,12,15

1

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

page 2 of 2

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

**Continuation of Box I.1**

Although claims 14 and 16 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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**Continuation of Box I.1**

Rule 39.1(iv) PCT – Method for treatment of the human or animal body by therapy

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 03/00499

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 03/00499

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 0232867		AU 25-04-2002	AU WO	9572301 A 0232867 A1		29-04-2002 25-04-2002
WO 9716440	A	09-05-1997	AT AU AU BR CA CZ DE DE EA WO EP ES GR HR HU IL JP JP NO NZ PL PT SI TR TW US US US ZA	188691 T 704155 B2 7493296 A 9611184 A 2234096 A1 9801322 A3 69606196 D1 69606196 T2 980404 A1 9716440 A1 0862566 A1 2143238 T3 3033154 T3 960507 A1 9802985 A2 123962 A 11514634 T 3073238 B2 981534 A 321575 A 327406 A1 862566 T 862566 T1 9800756 T2 460473 B 6197772 B1 6521621 B1 RE37886 E1 9609090 A		15-01-2000 15-04-1999 22-05-1997 30-03-1999 09-05-1997 16-09-1998 17-02-2000 21-09-2000 29-10-1998 09-05-1997 09-09-1998 01-05-2000 31-08-2000 28-02-1998 28-10-1999 11-01-2001 14-12-1999 07-08-2000 24-06-1998 28-05-1999 07-12-1998 30-06-2000 30-04-2000 21-07-1998 21-10-2001 06-03-2001 18-02-2003 15-10-2002 29-04-1998
WO 9724324	A	10-07-1997	AT AU AU BR CA CZ DE DE DK EA WO EP ES HK HU IL JP NO NZ PL PT SI SK TR US	206397 T 707037 B2 1308497 A 9612334 A 2238818 A1 9801864 A3 69615700 D1 69615700 T2 855999 T3 1559 B1 9724324 A1 0855999 A1 2164939 T3 1011205 A1 9904125 A2 124640 A 2000502690 T 982404 A 325843 A 327441 A1 855999 T 855999 T1 83198 A3 9801211 T2 6169097 B1		15-10-2001 01-07-1999 28-07-1997 02-03-1999 10-07-1997 16-12-1998 08-11-2001 05-09-2002 21-01-2002 23-04-2001 10-07-1997 05-08-1998 01-03-2002 08-03-2002 28-06-2000 23-05-2002 07-03-2000 19-08-1998 28-05-1999 07-12-1998 28-03-2002 31-12-2001 11-02-1999 21-09-1998 02-01-2001

Form PCT/ISA/210 (patent family annex) (July 1992)

page 1 of 2

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 03/00499

Patent document cited in search report	Publication date		Patent family member(s)	Publication date	
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